DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 23 December 2008 has been entered.

Response to Amendment

2. The amendment filed on 23 December 2008 does not place the application in condition for allowance.

Status of Rejections Pending Since the Office Action of 24 June 2008

3. The previous rejection of claims 1-3, 5-24, 26-38, 46-48, and 51 under 35 U.S.C. §112, second paragraph is withdrawn due to Applicant's amendment. New grounds under this statute are presented.

4. The rejection of claims 1-3, 5-24, 26-38, 46-48, and 51 under 35 U.S.C. §103(a) as unpatentable over Singh et al is maintained.

5. All other rejections are withdrawn due to Applicant's amendment.

Election/Restrictions

6. Claims 39-45 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 12 March 2008.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-3, 5-24, 26-38, 46-48, and 51 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. There is insufficient support in the specification as originally filed for the negative limitation requiring the device to be free of channels providing samples to the plurality of separation channels or to the separation channel. Note, for example, that each port 17 (Figures 4A-4G) as disclosed can be construed as a channel providing sample to the separation channels.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-3, 5-24, 26-38, 46-48, and 51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1 at line 17, it is unclear how the port can have a depth equal to an associated sidewall when the port is recited as being formed in the top wall. In the other independent claims 12, 30, 32, 46, 47, and 48, similar recitations of "an associated sidewall" are similarly unclear, since the port has been in all claims defined as being formed in one particular wall of the channel.

In addition, it is unclear how the instant devices can function without the disclosed channels 17 that provide samples to the plurality of separation channels. This limitation appears to exclude the ports claimed earlier in each independent claim, which are channels that function to provide samples to the separation channels, further rendering the claim indefinite.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 1-3, 5-24, 26-38, 46-48, and 51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Singh et al. (US Patent No. 6,627,406)

In this rejection, undue weight cannot be given to the recitation of “separation” channels or "separation" medium. Specifying an intended use, such as separation, does not structurally define the channels or medium. Therefore, channels having ports as claimed are considered to read on the claims, since they are structurally capable of performing separation, and aqueous medium is considered to read on the instant "separation medium", since it is capable of effecting separation of a sample via application of an electric field as claimed. (i.e. dissolved materials having different charge to mass ratios in an aqueous medium will separate under an applied electric field)

In addition, the limitation "wherein a sample to be separated is directly injected into the separation medium filling the plurality of separation channels through one or more of the virtual walls" corresponds only to intended use of the device and adds no further structural limitation to this device claim. The limitation is therefore considered to carry no patentable weight.

Furthermore, the limitation that the device be free of "sample" reservoirs and channels "providing samples to the plurality of separation channels" is also directed to the intended use of reservoirs and channels within a device. It is the Examiner's position that no reservoir of Singh is required to function as a "sample reservoir". Furthermore, no channel of Singh is required to "[provide] samples to the plurality of separation channels", other than the ports 612 that correspond to the ports instantly claimed. Accordingly, the device of Singh et al is considered to meet this limitation. Note that the fluid interface ports can be construed as "channels" in interpreting the claims, and the limitation therefore raises issues under 35 U.S.C. §112, 1st and 2nd paragraphs, as discussed in the corresponding rejections above.

Singh et al teach a separation device comprising one or more reservoirs (Figures 6A-6C; reservoirs 602, 604, or 606) and a plurality of channels connected to the reservoirs (608, 610) each channel having a first end connected to a reservoir and a second end connected to another reservoir (Top end of channel 610 is connected to reservoirs 602 and 604 via channel 608), each channel having an interior bounded by first and second side walls and top wall (or third sidewall) and bottom wall (or fourth sidewall) as claimed (Figures 6B and 6C show rectangular cross-sections meeting

these limitations); fluid interface ports (612) formed in the top wall of a channel, each port having a depth equal to a thickness of the top wall (which is "an associated sidewall"), and a diameter significantly larger than the depth (Example using system of Figure 6; Column 34, line 65 - Column 35, line 17); wherein an aqueous medium disposed in the channel forms a virtual wall at the fluid interface port and no medium enters the fluid interface port. (Column 29, lines 6-14; port walls are not wettable, aqueous medium does not rise up the walls) Singh et al teach several channel systems with reservoirs multiplexed to numerous channels. (e.g. Figures 3 and 9-11) Regarding claims 14, 15, and 21, the devices of Singh et al are disclosed as being made from a glass or plastic plate having channels formed therein and a cover plate of the same or different material. (Column 12, lines 36-43)

Singh et al do not explicitly disclose the reservoirs of Figure 6 being anode or cathode reservoirs, nor do they explicitly teach channels multiplexed to reservoirs in the system of Figure 6. Regarding claim 12, Singh et al do not explicitly disclose the arrays of reservoirs in the system of Figure 6.

Singh et al teach the optional provision of electrodes to the reservoirs of their systems for providing electrokinetic fluid motion. (Column 21, lines 8-25 and Column 22, lines 32-50) Singh et al also teach multiplexing the channels of their systems (e.g. Figures 3 and 9-11; Column 6, lines 17-38) to provide flexibility in operation, such as delivery of agents to zones for reaction. Regarding claim 12, Singh et al also teach providing a plurality of channel systems in an array on a substrate. (Figures 11-14) Regarding claim 39, Singh et al disclose forming droplets and directing these droplets of

liquid to a zone to make immediate contact with fluid in the channels. (Column 7, line 66 - Column 8, line 5)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the system of Figure 6 of Singh et al by providing electrodes to the reservoirs, as suggested by Singh et al, because it would provide the ability to manipulate the fluids in the device electrokinetically, as suggested by Singh et al (Column 21, lines 8-25 and Column 22, lines 32-50)

It would also have been obvious to one having ordinary skill in the art at the time the invention was made to modify the system of Figure 6 of Singh et al by multiplexing the channels to numerous other channels and reservoirs, as suggested by Singh et al, because Singh et al teach that this provides desirable flexibility in operation, such as in delivery of different materials to zones for reaction. (Figures 3 and 9-11; Column 6, lines 17-38)

Such provision of electrodes and multiplexing of the channel systems meets the limitations to independent claims 1, 30, 32, 40, 43, and 46-48.

Specific to claim 12, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the device of Figure 6 of Singh et al by providing an array of devices on a single substrate, as shown by Singh et al in Figures 11-14, because such a device geometry would allow facile parallel analyses, the advantageousness of which would have been apparent to anyone having ordinary skill in the art of biochemical analysis.

Regarding claims 2, 16, 22, 24, and 34, Singh et al suggest such an array. (Column 22, lines 33-40)

Regarding claim 3, the multiplexed systems connect outer regions to inner regions. (Figures 3 and 9-11)

Regarding claim 5, with no fluid travel into ports 612, the dead volume will be zero. (Column 29, lines 7-9)

Regarding claims 6 and 23, Figures 6a and 6c show such an array of ports.

Regarding claims 7, 13, 31, and 33, such choice of size with no change in device operation does not result in patentable distinction over the prior art. In *Gardner v. TEC Systems, Inc.*, 725 F.2d 1338, 220 USPQ 777 (Fed. Cir. 1984), *cert. denied*, 469 U.S. 830, 225 USPQ 232 (1984), the Federal Circuit held that, where the only difference between the prior art and the claims was a recitation of relative dimensions of the claimed device and a device having the claimed relative dimensions would not perform differently than the prior art device, the claimed device was not patentably distinct from the prior art device.

Regarding claims 8-11 and 26-29, Singh et al disclose the systems performing such a variety of analyses. (Column 22, lines 51-55; Column 21, lines 13-25) Regardless, the recitation of an intended use of the device does not further structurally define the device, and the claims are rendered obvious for the reasons given for claims 1 and 12.

Regarding claims 17 and 19, Singh et al also suggest an electrode array integral to the two substrates. (Column 22, lines 33-40; “painting” electrodes) Such an array

would have a particular alignment relative to the reservoirs and ports as claimed in claim 19.

Regarding claims 18 and 35-37, Figures 6a and 6c show regular spacing of the ports. The limitation to a loading device, such as a pipetter or pin, corresponds to intended use, and cannot be given significant weight. The arrangement shown in the figures is considered to be “configured” or “adapted” appropriately for such use.

Regarding claim 20, Figure 6 shows only holes that are reservoirs, which could obviously have electrodes (i.e. anodes or cathodes) as discussed above, or ports. Singh et al disclose adding samples to each port. (Column 29, lines 9-11) Therefore, the number of holes is as claimed.

Regarding claim 38, choice of a radial or other conventional channel pattern is a matter of design choice to a skilled artisan based on which design is most suitable for the peripheral devices to be used with the system. In the absence of evidence that the shape is significant to system operation, such selection of shape does not confer patentability. For instance, in *In re Dailey*, 357 F.2d 669, 149 USPQ 47 (CCPA 1966), the court held that the configuration of the claimed object was a matter of choice which a person of ordinary skill in the art would have found obvious absent persuasive evidence that the particular configuration of the claimed container was significant.

Regarding claim 51, Singh et al teach a droplet generating system including a pin corresponding to the fluid interface port as claimed. (Column 9, lines 11-19)

15. Claims 1-3, 5-11, and 46-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heller et al (WO 99/64850) in view of Singh et al and either McCormick et al or Amigo. Since WO 99/64850 is in German, citations below are given to US Patent No. 6,846,398, which issued from the National Stage entry of this International Application.

In this rejection, undue weight cannot be given to the recitation of “separation” channels or "separation" medium. Specifying an intended use, such as separation, does not structurally define the channels or medium. Therefore, channels having ports as claimed are considered to read on the claims, since they are structurally capable of performing separation, and aqueous medium is considered to read on the instant "separation medium", since it is capable of effecting separation of a sample via application of an electric field as claimed. (i.e. dissolved materials having different charge to mass ratios in an aqueous medium will separate under an applied electric field)

In addition, the limitation "wherein a sample to be separated is directly injected into the separation medium filling the plurality of separation channels through one or more of the virtual walls" corresponds only to intended use of the device and adds no further structural limitation to this device claim. The limitation is therefore considered to carry no patentable weight.

Furthermore, the limitation that the device be free of "sample" reservoirs and channels "providing samples to the plurality of separation channels" is also directed to the intended use of reservoirs and channels within a device. It is the Examiner's

position that no reservoir of Heller et al is required to function as a "sample reservoir". Furthermore, description of the way in which the channels are to be used provides no structural distinction from Heller et al. Accordingly, the device of Heller et al is considered to meet this limitation. Note that the fluid interface ports can be construed as "channels" in interpreting the claims, and the limitation therefore raises issues under 35 U.S.C. §112, 1st and 2nd paragraphs, as discussed in the corresponding rejections above.

Relevant to claims 1 and 46-48, Heller et al disclose a separation device (Figures 1 and 2) comprising: anode and cathode reservoirs (P1 and P2); a plurality of channels (i.e. sections of I lying between channels S) having respective ends connected to the anode and cathode reservoirs (e.g. all sections of channel I are connected to these reservoirs via channels S); a plurality of interface ports (A) formed in the sidewalls of the channels to provide access to the channels, each of the ports having a depth equal to the cover thickness (Column 6, lines 1-2); with the anode and cathode reservoirs multiplexed with the channels. (Figure 1)

Relevant to claim 2, Heller et al disclose an electrode array coupled or coupleable to the reservoirs and fluid inlets within the separation device. (Figure 1; Electrodes E1-E4)

Relevant to claim 3, the device of Heller et al has an outer perimeter (Figure 1), and the plural channel sections of channel I connect a portion of this perimeter to the center of the device.

Relevant to claim 6, Heller et al disclose such an array of apertures (Figures 1 and 2)

Relevant to claim 7, Heller et al disclose channel widths of 20 - several hundred microns, and the port diameter is bounded by the channel width. (Figure 2; Column 4, lines 61-62; Column 5, lines 21-25)

Relevant to claim 8, Heller et al disclose their device being a capillary array electrophoresis plate. (Figure 1; Column 1, lines 5-10)

Regarding the independent claims, a meniscus will form at interface ports A. Such menisci will inherently exist in this device filled with a flowable separation medium (i.e. buffer).

Heller et al do not explicitly disclose the thickness of their cover, which is pertinent to the dimensional limitations of the instant claims, an interface port wider than it is deep, or a “virtual wall” meniscus. Heller et al are also silent concerning the instant channel shapes, and whether three walls other than the top wall (i.e. cover) are present as claimed.

McCormick et al disclose a microfluidic system similar in construction to that of Heller et al, in which they cover the channels with a cover as thin as 10 microns. (Column 13, lines 17-22)

Amigo discloses a microfluidic system similar in construction to that of Heller et al, in which they cover the channels with a cover as thin as 10 microns. (Column 8, lines 1-6)

Singh et al is cited as teaching a conventional channel shape for microfluidic devices. Each channel of Singh et al has an interior bounded by first and second side walls and top wall (or third sidewall; corresponds to the cover of Heller et al.) and bottom wall (or fourth sidewall) as claimed (Figures 6B and 6C show rectangular cross-sections meeting these limitations)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the device and methods of Heller et al by specifically using a cover as thin as 10 microns, as taught by either McCormick et al or Amigo, because the silence of Heller et al concerning this indicates that a skilled artisan could choose any suitable cover thickness such as those known in the prior art, e.g. McCormick et al or Amigo. The choice of thinner material could be motivated by reduction of material consumption, which could potentially reduce manufacturing costs.

It would also have been obvious to one having ordinary skill in the art to choose any conventional channel cross-sectional shape, such as the rectangular channels shown by Singh et al, because Singh et al demonstrates the suitability of these channels for such microfluidic systems. Such choice of channel shape would only have led to the predictable result of a functional microfluidic device.

Regarding the independent claims, within this combination, with a channel and port width of twenty to hundreds of microns (Heller et al; Column 4, lines 61-62; Figure 2) and cover thickness of 10 microns, the limitation to a port diameter significantly larger than its depth is met.

Regarding the limitations to a “virtual wall” and requiring that "no separation medium enters the fluid interface port", Heller et al provide no explicit disclosure except that all channels in their system are filled with a separation medium, and therefore a medium/air interface will exist at these ports. Whether the medium forms a meniscus at the interior or exterior surface of the port depends on the cross-sectional area of the port vs. that of the channel - fluid will naturally be drawn into the narrower opening, driven by its surface tension. While no explicit channel depth is recited by Heller, a shallow channel could obviously be used (See figure 6 of Singh et al, for example - such a shape is conventional in the art). In the absence of applied pressure, fluid in the channel would not be drawn into the port to a significant extent, and the meniscus would form at the bottom surface of the wall, leading to no medium entering the port, and a port dead volume of substantially zero. Given a conventional flowable separation medium (e.g. buffer), this meniscus would correspond to the instantly claimed “virtual wall”, as no distinction between the respective ports, associated channels, or fluids can be seen.

Specific to claims 9-11, such limitations to intended use of a system do not further structurally define the claimed device, and the claims are therefore rendered obvious for the same reasons cited above regarding claim 1.

16. Claims 12-24 and 26-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heller et al in view of Bjornson et al (US 6,284,113) and either McCormick et al or Amigo.

In this rejection, undue weight cannot be given to the recitation of “separation” channels or "separation" medium. Specifying an intended use, such as separation, does not structurally define the channels or medium. Therefore, channels having ports as claimed are considered to read on the claims, since they are structurally capable of performing separation, and aqueous medium is considered to read on the instant "separation medium", since it is capable of effecting separation of a sample via application of an electric field as claimed. (i.e. dissolved materials having different charge to mass ratios in an aqueous medium will separate under an applied electric field)

In addition, the limitation "wherein a sample to be separated is directly injected into the separation medium filling the plurality of separation channels through one or more of the virtual walls" corresponds only to intended use of the device and adds no further structural limitation to this device claim. The limitation is therefore considered to carry no patentable weight.

Furthermore, the limitation that the device be free of "sample" reservoirs and channels "providing samples to the plurality of separation channels" is also directed to the intended use of reservoirs and channels within a device. It is the Examiner's position that no reservoir of Heller et al is required to function as a "sample reservoir".

Furthermore, description of the way in which the channels are to be used provides no structural distinction from Heller et al. Accordingly, the device of Heller et al is considered to meet this limitation. Note that the fluid interface ports can be construed as "channels" in interpreting the claims, and the limitation therefore raises issues under 35 U.S.C. §112, 1st and 2nd paragraphs, as discussed in the corresponding rejections above.

Relevant to claim 12, Heller et al disclose a separation device (Figures 1 and 2) comprising: an array of microfabricated channel sections (Portions of I positioned between channels S) formed in a substrate and covered by a cover (Column 5, lines 10-12; Column 6, lines 1-2), anode and cathode reservoirs (P1, P2, reservoirs for E3, E4); the channel sections having respective ends connected to the anode and cathode reservoirs (e.g. all sections of channel I are connected to the reservoirs via channels S and other channel sections of I) an array of interface ports (A) formed in the sidewalls of the channels to provide access to the channel, each of the ports having a depth equal to the sidewall (i.e. cover) thickness (Column 6, lines 1-2); with the anode and cathode reservoirs connected at the ends of the channels. (Figure 1)

Relevant to claim 13, Heller et al disclose channel widths of 20 - several hundred microns, and the port diameter is bounded by the channel width. (Figure 2; Column 4, lines 61-62; Column 5, lines 21-25)

Relevant to claims 16 and 22, Heller et al disclose an electrode array coupled or coupleable to the reservoirs and fluid inlets within the separation device. (Figure 1; Electrodes E1-E4)

Relevant to claim 18, Heller et al disclose such a regularly-spaced array of apertures (Figures 1 and 2; regular spacing of ports would be provided for the regularly spaced channels)

Relevant to claim 20, the combined number of ports and application areas/holes in Heller et al is as claimed.

Relevant to claim 23, Heller et al show a plurality of ports in channel I. (Figures 1 and 2)

Relevant to claim 26, Heller et al disclose their device being a capillary array electrophoresis plate. (Figure 1; Column 1, lines 5-10)

Regarding the independent claims, a meniscus will form at interface ports A. Such menisci will inherently exist in this device filled with a flowable separation medium (i.e. buffer).

Heller et al do not explicitly disclose the thickness of their cover, which is pertinent to the dimensional limitations of the instant claims, an interface port wider than it is deep, a “virtual wall” meniscus, or arrays of anode and cathode reservoirs as claimed. Heller et al are also silent concerning the instant channel shapes, and whether three walls other than the top wall (i.e. cover) are present as claimed.

McCormick et al disclose a microfluidic system similar in construction to that of Heller et al, in which they cover the channels with a cover as thin as 10 microns. (Column 13, lines 17-22)

Amigo discloses a microfluidic system similar in construction to that of Heller et al, in which they cover the channels with a cover as thin as 10 microns. (Column 8, lines 1-6)

Bjornson et al teach the benefits of highly parallel analyses made possible by providing a large number of microfluidic electrophoresis systems in a single chip. (Figures 6-8; Column 25, line 37 - Column 26, line 54)

Singh et al is cited as teaching a conventional channel shape for microfluidic devices. Each channel of Singh et al has an interior bounded by first and second side walls and top wall (or third sidewall; corresponds to the cover of Heller et al.) and bottom wall (or fourth sidewall) as claimed (Figures 6B and 6C show rectangular cross-sections meeting these limitations)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the device and methods of Heller et al by specifically using a cover as thin as 10 microns, as taught by either McCormick et al or Amigo, because the silence of Heller et al concerning this indicates that a skilled artisan could choose any suitable cover thickness such as those known in the prior art, e.g. McCormick et al or Amigo. The choice of thinner material could be motivated by reduction of material consumption, which could potentially reduce manufacturing costs.

It would also have been obvious to one having ordinary skill in the art at the time the invention was made to modify the device of Heller et al by providing a chip having an array of the microfluidic devices of Heller et al, as taught by Bjornson et al, because

Bjornson et al teach the desirability of parallel analyses being performed in an array of microfluidic devices on a single substrate. The desirability of such parallel capability would have been obvious to a skilled artisan. Such modification meets the claim limitation that each channel is connected to the respective arrays of anode and cathode reservoirs by virtue of them being connected to at least two reservoirs that are part of the array provided by the combination.

It would also have been obvious to one having ordinary skill in the art to choose any conventional channel cross-sectional shape, such as the rectangular channels shown by Singh et al, because Singh et al demonstrates the suitability of these channels for such microfluidic systems. Such choice of channel shape would only have led to the predictable result of a functional microfluidic device.

Regarding claim 12, within this combination, with a channel and port width of twenty to hundreds of microns (Heller et al; Column 4, lines 61-62; Figure 2) and cover thickness of 10 microns, the limitation to a port diameter significantly larger than its depth is met.

Regarding the limitations to a “virtual wall” and requiring that "no separation medium enters the fluid interface port", Heller et al provide no explicit disclosure except that all channels in their system are filled with a separation medium, and therefore a medium/air interface will exist at these ports. Whether the medium forms a meniscus at the interior or exterior surface of the port depends on the cross-sectional area of the port vs. that of the channel - fluid will naturally be drawn into the narrower opening, driven by its surface tension. While no explicit channel depth is recited by Heller, a

shallow channel could obviously be used (See figure 6 of Singh et al, for example - such a shape is conventional in the art). In the absence of applied pressure, fluid in the channel would not be drawn into the port to a significant extent, and the meniscus would form at the bottom surface of the wall, leading to no medium entering the port, and a port dead volume of substantially zero. Given a conventional flowable separation medium (e.g. buffer), this meniscus would correspond to the instantly claimed “virtual wall”, as no distinction between the respective ports, associated channels, or fluids can be seen.

Specific to claims 27-29, such limitations to intended use of a system do not further structurally define the claimed device, and the claims are therefore rendered obvious for the same reasons cited above regarding claim 12.

Specific to dependent claims 14, 15, and 21:

In addition to the obviousness arguments made above, Heller et al do not teach the particular materials claimed. Heller et al are silent concerning the materials from which their devices are formed.

Bjornson et al teach making microfluidic devices from glass, plastic, or a combination thereof. (Column 21, lines 35-43)

It would have been obvious to one having ordinary skill in the art to modify the system of Heller et al by forming the device from glass, plastic, or a mixture thereof, as taught by Bjornson et al, because Bjornson et al teach that such materials are suitable for making microfluidic devices for electrophoresis. The silence of Heller et al on this

subject would have caused a skilled artisan to turn to the related prior art, such as Bjornson et al, for teaching of proper materials.

Specific to dependent claims 17, 19, and 24:

In addition to the obviousness arguments made above, Heller et al do not teach electrodes integral to the substrates.

Bjornson et al teach depositing electrodes directly on a microfluidic device, in contact with the reservoirs thereof. (Column 20, lines 39-45)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the system of Heller et al by providing electrodes deposited directly on the substrate in contact with the reservoirs, as taught by Bjornson et al, because this would eliminate the need for manufacture of a separate electrode plate, and simplify electrical connection to the fluids within the device by eliminating concerns regarding precise alignment. Such deposited arrays meet the limitations of these claims.

17. Claims 1-3, 5-8, 12-24, 26, 30-36, 38, and 46-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Simpson et al in view of Singh et al and Howitz et al.

In this rejection, undue weight cannot be given to the recitation of “separation” channels or "separation" medium. Specifying an intended use, such as separation, does not structurally define the channels or medium. Therefore, channels having ports as claimed are considered to read on the claims, since they are structurally capable of

performing separation, and aqueous medium is considered to read on the instant "separation medium", since it is capable of effecting separation of a sample via application of an electric field as claimed. (i.e. dissolved materials having different charge to mass ratios in an aqueous medium will separate under an applied electric field)

In addition, the limitation "wherein a sample to be separated is directly injected into the separation medium filling the plurality of separation channels through one or more of the virtual walls" corresponds only to intended use of the device and adds no further structural limitation to this device claim. The limitation is therefore considered to carry no patentable weight.

Furthermore, the limitation that the device be free of "sample" reservoirs and channels "providing samples to the plurality of separation channels" is also directed to the intended use of reservoirs and channels within a device. It is the Examiner's position that no reservoir of the combination made herein is required to function as a "sample reservoir". Furthermore, description of the way in which the channels are to be used provides no structural distinction. Accordingly, the device taught by the prior art is considered to meet this limitation. Note that the fluid interface ports can be construed as "channels" in interpreting the claims, and the limitation therefore raises issues under 35 U.S.C. §112, 1st and 2nd paragraphs, as discussed in the corresponding rejections above.

Relevant to claim 1, Simpson et al disclose a separation device (Column 1, line 65 - Column 2, line 1) comprising: one or more anode reservoirs (Figure 1, 180;

Column 9, lines 25-27)); a plurality of separation channels connected to the anode reservoirs (Column 3, lines 14-28; Column 9, lines 25-27), with each of the separation channels having an interior bounded by a side wall (Figure 4B; Column 4, line 47 - Column 5, line 7); each separation channel having first and second ends connected to anode and cathode reservoirs as claimed (Figures 1 and 2); a plurality of fluid inlets to the separation channels (Figure 2, B and C with associated channels to channel 222); and at least one cathode reservoir multiplexed with two or more separation channels. (Figure 1, Reservoir 120)

Relevant to claim 12, Simpson et al disclose a separation device comprising: an array of microfabricated separation channels formed at the surface of a first microfabricated substrate and a corresponding surface of a second substrate bonded to the surface of the first substrate with each channel having an interior bounded by a sidewall, a first end and a second end connected to anode and cathode reservoirs as claimed (Figures 1 and 4B; Column 9, lines 12-17; Column 4, line 47 - Column 5, line 7); an array of fluid inlets to the separation channels (Figures 1 and 2, B and C with associated channels to channel 222); an array of cathode reservoirs connected to the first end of each of the separation channels (Figure 1; Column 9, lines 23-24); and an array of anode reservoirs, wherein at least one anode reservoir is connected to the respective second ends of at least two of the separation channels. (Figure 1; Column 9, lines 25-27)

Relevant to claims 30 and 32, Simpson et al disclose a separation device comprising: a substrate (Column 4, line 47 - Column 5, line 7); a plurality of separation

channels formed in the substrate (Column 3, lines 14-28), each channel having an interior bound by a side wall (Figure 4B; Column 4, line 47 - Column 5, line 7); each separation channel having first and second ends connected to anode and cathode reservoirs as claimed (Figures 1 and 2); a plurality of fluid inlets to the separation channels (Figure 2, B and C with associated channels to channel 222); an anode reservoir multiplexed to two or more separation channels (Figure 1, Reservoir 180; Column 10, lines 49-57); and a cathode reservoir multiplexed to two or more separation channels (Figure 1, Reservoir 120; Column 10, lines 58-65)

Relevant to claims 2, 16, 17, 22, and 34, Simpson et al disclose an electrode array coupled or coupleable to the reservoirs and fluid inlets within the separation device. (Column 5, line 36 - Column 6, line 37; Column 10, lines 9-10) This array can be in electrical contact with the device (Figure 4B; Column 10, lines 31-33), or integral with the substrates of the device (Column 10, lines 11-13).

Relevant to claim 3, Simpson et al disclose a separation device with an outer perimeter and a center, with the separation channels connecting the outer perimeter to the center. (Figure 9; Column 9, lines 9-11)

Relevant to claims 8 and 26, Simpson et al disclose their device being a capillary array electrophoresis plate. (Column 1, lines 65-66)

Relevant to claim 14, Simpson et al disclose the first and second substrates being made of glass. (Column 9, lines 66-67)

Relevant to claim 15, Simpson et al disclose the first and second substrates being made of plastic. (Column 10, lines 1-2)

Relevant to claims 18 and 35, Simpson et al disclose the regular spacing of the fluid inlets on one of the substrates to receive solutions from a parallel loading device. (Column 1, lines 13-15; Column 4, line 47 - Column 5, line 7)

Relevant to claims 19 and 24, Simpson et al disclose the first substrate of their device including an array of electrodes aligned with sample reservoirs of the device to make electrical contact with solutions in the sample, waste, anode, and cathode reservoirs. (Column 10, lines 17-23)

Relevant to claim 20, Simpson et al disclose a number of holes, H, approximately equal to 5N/4, where N is the number of samples to be processed. (Column 10, lines 24-27)

Relevant to claim 21, Simpson et al disclose their device being made of a combination of glass and plastic. (Column 10, lines 28-30)

Relevant to claim 23, Simpson et al disclose a plurality of sample fluid inlets in communication with on of the separation channels (e.g. Figure 2, B and C both feed channel 222)

Relevant to claim 36, Simpson et al disclose a parallel loading device comprising a multi-headed pipetter. (Column 11, lines 16-18)

Relevant to claim 38, Simpson et al disclose the disposition of the separation channels in a radial pattern on the separation device. (Figure 9)

Simpson et al do not explicitly disclose a device comprising: fluid interface ports formed in the side walls of the separation channels to provide access to the interiors of

the separation channels, wherein the diameter of the port is significantly larger than its depth, wherein a separation medium disposed in the interior of the separation channel forms a virtual wall at each fluid interface port, and wherein no separation medium enters the fluid interface port (Claim 1), zero dead volume (Claim 5), or diameters between 25 and 125 μm. (Claims 7, 13, 25, 31, 33) They also do not explicitly disclose a fluid interface port that comprises an array of apertures forming virtual walls. (Claim 6) They also do not teach a channel specifically having the four walls of the claim.

Howitz et al disclose a device (Figure) comprising: fluid interface ports (capillaries containing menisci 6) formed in the side wall of a fluid channel (9) to provide access to the interior of the fluid channel, wherein a separation medium disposed in the interior of the fluid channel forms a virtual wall at each fluid interface port (Menisci 6). (Column 3, lines 11-15) Relevant to claim 6, they also disclose a fluid interface port comprising an array of apertures forming virtual walls.

Singh et al is cited as teaching a conventional channel shape for microfluidic devices. Each channel of Singh et al has an interior bounded by first and second side walls and top wall (or third sidewall; corresponds to the cover of Heller et al.) and bottom wall (or fourth sidewall) as claimed (Figures 6B and 6C show rectangular cross-sections meeting these limitations)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the device of Simpson et al by replacing the sample and

waste reservoirs, and their associated side channels with a simple hole or holes through the sidewall to serve as a fluid port, as taught by Howitz et al, because Howitz et al teach the usefulness of their fluid port in introducing fluids to microchannels while preventing outflow of the fluid contained within the channel. (Column 1, lines 53-58) It would also reduce the number of holes required in the device by eliminating the need for injection crosses, this reduction in the number of holes having been taught by Simpson et al to be desirable. (Column 3, lines 50-65)

Further addressing claims 1 and 5, given the definition of dead volume presented in the instant specification (roughly, the volume of liquid held in the port and not flowing with the fluid within the channel), the dead volume associated with ports such as those of Howitz et al will be variable, as a function of the affinities of the fluids for the surface of the port, among other factors. (Column 3, lines 25-31) As such, the dead volume will be zero or near zero (i.e. no fluid enters the port) for a clean hydrophobic port surface in a device using aqueous fluids. Such hydrophobicity is an innate property of many polymers known to be useful in manufacturing microfluidic devices (e.g. fluoropolymers) or it could be achieved by using known surface treatments for glass (hexamethyldisilazane, used by Simpson - Column 4, lines 53-56) and silicon (Hydrofluoric acid), and would constitute an obvious modification of the device, because such a surface would minimize loss of the injected sample. (i.e. if an aqueous sample hit a hydrophobic surface in a port configured in the way shown in the Figure of Howitz et al, substantially the entire droplet would immediately fall into contact with the fluid in

channel 9, as the contact angle and reduced frictional force would not be sufficient to retain the droplet on this surface)

Regarding the limitation that the port is wider than it is deep, although the example given by Howitz et al does not meet this limitation, Howitz et al also disclose variation of the depth of the port. (i.e. length of the capillary; Column 2, lines 5-10 and 27-30) Choice of a shorter length such that this limitation is met would have been obvious to a skilled artisan, particularly given the trend towards miniaturization in this art.

It would also have been obvious to one having ordinary skill in the art to choose any conventional channel cross-sectional shape, such as the rectangular channels shown by Singh et al, because Singh et al demonstrates the suitability of these channels for such microfluidic systems. Such choice of channel shape would only have led to the predictable result of a functional microfluidic device.

Further addressing claim 20, by replacing each sample reservoir with a fluid interface port, and eliminating waste reservoirs, the number of holes in this combination device would be reduced to N+A+C, where N is the number of samples to be analyzed, A is the number of anode reservoirs, and C is the number of cathode reservoirs.

Regarding claims 46-48, each of these claims fully encompasses claim 1 in that they only recite limitations that are present in claim 1, while removing various other limitations. The prior art as applied to claim 1 above therefore also renders these claims obvious, given their open language (i.e. “comprising”).

18. Claims 9-11 and 27-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Simpson et al, Singh et al, and Howitz et al as applied to claims 1-3, 5-8, 12-24, 26, 30-36, 38, and 46-48 above, and further in view of Bjornson et al. (US 6,103,199)

Simpson et al, Singh et al, and Howitz et al disclose combinations as described above in addressing claims 1-3, 5-8, 12-24, 26, 30-36, 38, and 46-48.

None among Simpson et al, Singh et al, and Howitz et al disclose their devices being used for electrochromatography (Claims 9 and 27), pressure-driven chromatography (Claims 10 and 28), or isoelectric focusing (Claims 11 and 29).

Bjornson et al disclose electrophoretic devices used for isoelectric focusing and capillary chromatography. (Column 12, lines 53-59) They also disclose fluid flow in their devices by electroosmosis (Column 11, lines 55-60), which suggests electrochromatography. (i.e. chromatography in which the motion of the mobile phase is caused by an electric field)

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the combination of Simpson et al, Singh et al, and Howitz et al by providing the separation capillaries with a chromatographic medium, immobilized pH gradient, or ampholytes and using the device for electrochromatography or isoelectric focusing, as taught by Bjornson et al, because it would provide useful analytical data about the analytes. It would be well within the abilities of one having ordinary skill in the art to use the channel structure shown by Simpson et al with any known prior art capillary electrophoretic technique, such as those claimed here.

Additionally, electroosmotic force corresponds to a type of pressure driving a fluid through a capillary, and as such, is considered a form of pressure-driven chromatography.

19. Claims 37 and 51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Simpson et al, Singh et al, and Howitz et al as applied to claims 1-3, 5-8, 12-24, 26, 30-36, 38, and 46-48 above, and further in view of Sundberg et al.

Simpson et al, Singh et al, and Howitz et al disclose a combination as described above in addressing claims 1-3, 5-8, 12-24, 26, 30-36, 38, and 46-48.

None among Simpson et al, Singh et al, and Howitz et al disclose a parallel loading device comprising a pin corresponding to a fluid interface port and for carrying and introducing the droplet of a liquid sample to the fluid interface port by contacting the virtual wall.

Sundberg et al disclose a parallel loading device (Figure 2) comprising a pin (38) for carrying and introducing the droplet of a liquid sample (36) to the ports (34) of a microfluidic system.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the combination of Simpson et al, Singh et al, and Howitz et al by providing a parallel loading device comprising pins for carrying liquid samples to the fluid interface port, as taught by Sundberg et al, because it would simplify delivery of small droplets. It would be well within the abilities of one having ordinary skill in the art to choose any known means of delivering fluid droplets to a selected spot in a

microfluidic device (i.e. the port), such as that taught by Sundberg et al. A technique that delivers a plurality of droplets simultaneously, such as that of Sundberg et al, would be particularly obvious to choose, because it would aid in increasing throughput, decreasing labor, etc.

Response to Arguments

20. Applicant's arguments filed 23 December 2008 have been fully considered but they are not persuasive.

Applicant argues that the claims now require the channel ends to be connected to the anode/cathode reservoirs, and that Singh et al does not meet this limitation. The Examiner respectfully disagrees, since the channels of Singh et al have ends that are clearly connected to such reservoirs, either directly or via other channels.

Applicant further argues that the claims require a medium that can "effect separation of a sample in the separation medium via application of an electric field across the plurality of separation channels", and that such limitation must be given weight. The examiner agrees that this recitation limits the claim to a material that can perform the intended use, but maintains that a simple aqueous buffer, such that taught in the prior art references meets this limitation, because materials having different charge-to-mass ratios in such aqueous buffers will undergo separation upon application of an electric field.

Applicant's further arguments concerning Singh's channels not being separation channels are not persuasive, since as noted above, the channels are connected to

reservoirs, and as put forth in the rejection, it would have been obvious to provide anodes and cathodes to the reservoirs. Comments on how the instant device may operate differently that that of Singh et al are irrelevant, since no particular weight can be given to the way in which the device is intended to be used. For the same reason, arguments concerning the way in which Applicant proposes to introduce sample to the device are not persuasive, since they bear no relevance to the structure defined by the claim.

Applicant further argues that the channels of Heller that have application areas A are used for injection as opposed to separation. Again, arguments concerning the function of the device do not define structure distinct from the prior art, and the Examiner again notes that an aqueous medium present in the sections of channel I meets the limitation to the instant "separation medium". The prior art is considered to meet the claim limitations for the detailed reasons given in the rejection.

Applicant argues that the references do not disclose a fluid interface port forming a virtual wall that replaces a removed portion of a side wall or a meniscus that is co-planar with a side wall of a channel. The references teach media filling channels having ports that are structurally the same as those instantly disclosed and claimed. In the absence of any evidence to the contrary, the Examiner maintains that fluids will behave in these systems in the same way they behave in Applicant's system. Any recited limitations that merely describe the way in which a fluid behaves in a channel having a hole in its side must be considered inherent over the structures taught, for example, by Heller et al or Singh et al, because the channel/port structures taught by these

references are the same as those instantly claimed. Once liquid is added to the channels, the liquid must be considered to behave precisely the same as long as there is no structural difference between the claims and the prior art. Applicant must claim structure that distinguishes the claimed subject matter from the prior art in order for the claims to be allowable.

Applicant argues that the "microdiode" of Howitz is not equivalent to "holes through the sidewall of a channel". Applicant is invited to elaborate, but the Examiner notes that the "microdiode" is taught by Howitz as a means for introducing fluids into a channel, and is relied upon for this teaching. Modification of Simpson to replace the sample introduction means as proposed would result in holes in the top/side wall of the channel of Simpson, which would appear to correspond to the claimed structure.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Jeffrey T. Barton whose telephone number is (571)272-1307. The examiner can normally be reached on M-F 9:00AM - 5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nam Nguyen can be reached on (571) 272-1342. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jeffrey T. Barton/
Examiner
Art Unit 1795
27 February 2009